THE REJECTIONS

1. Claims 1-11 are rejected under 35 USC § 112, second paragraph, as veing vague and indefinite.

2. Claims 1-11 are rejected under 35 USC § 103(a) as being unpatentable over Anderson et al. (hereinafter "Anderson") further in view of Stimpel et al. (hereinafter "Stimpel).

REMARKS

1. Claims 1-11 have been rejected under 35 USC § 112, second paragraph, as being vague and indefinite in the recitation of an "effective" immunization dosage. Apparently, the Examiner believes that one of skill in the art would not be able to determine the metes and bounds of such a limitation. Accordingly, the claim has been amended to recite an "effective amount" which is believed to be consistent with vaccine-related claim language in the patent literature.

Moreover, it is pointed out that anticoccidial vaccines are numerous and known in the art, and the amount used would depend on the vaccine utilized. As discussed in the specification, for

example on page 3, Background of the Invention, a "number of vaccines have been developed, including both live (virulent and attenuated), antigenic components and various recombinants" and, on page 10, Detailed Description of the Invention, the "vaccine utilized may be any which is effective against coccidial parasites, and administration of the vaccine should be carried out as appropriate for the particular vaccine selected." A commercially available vaccine, Immunocox®, is also mentioned as effective. In view of the extensive amount of information which is available and referred to in the specification, it is believed that one of skill in the art would have no trouble discerning what would constitute an effective amount of a particular vaccine.

For these reasons, it is believed that the claims are clear and definite, and it is respectfully requested that the rejection be withdrawn.

2. Claims 1-11 have been rejected under 35 USC § 103(a) as being unpatentable over Anderson in view of Stimpel.

As stated by the Examiner, the Anderson reference teaches the protection of poultry against coccidiosis by vaccination with

an anticoccidial vaccine. Anderson, however, does not teach providing an *Echinacea* supplement to enhance the immune response to the vaccine. Stimpel is relied upon to fill that gap, allegedly because the reference teaches that "Echinacea purpurea strongly activates the immune system of animals" and that "the compound may be of therapeutical interest". Applicants respectfully disagree with the Examiners' interpretation of the Stimpel reference and its combination with Anderson for the following reasons.

First, Stimpel does not teach that *E. purpurea* strongly activates the immune system of animals. It is specifically stated in the Abstract that "(p)urified polysaccharides (EPS) prepared from the plant *Echinacea purpurea* are shown to strongly activate macrophages." EPS is only one compound isolated from the plant, and applicants utilize the whole plant, not just one compound extracted from the plant. As shown in Table 1, there are several constituents in *Echinacea* products, i.e. chicoric acid, polysaccharides, isobutylamides and polyphenols. It is unknown which and to what degree the constituents are involved in the critical role, and to attribute all the beneficial activity to one purified fraction is unsubstantiated by anything presented

by Stimpel. Furthermore, EPS activates macrophages, not the immune system. The immune system is considerably more complex than macrophages alone, and there was evidence presented that showed that important components of the immune system (e.g. T cells and B cells) were either not stimulated at all (T cells) or only weakly stimulated (B cells). Moreover, there was speculation that the weak response of B cells was due to contamination by macrophages. Both of these systems could be expected to play a role in the enhancement of an immune response.

Second, all experimentation by Stimpel was carried out in *in vitro* tests using macrophages obtained from mice. Not only is an *in vitro* response not necessarily accurately predictive of *in vivo* response, a mammalian response is not necessarily indicative of an avian response, and the invention is specifically directed to the *in vivo* treatment of poultry. The Examiner's attention is drawn to the last sentence of the reference where Stimpel states that "(f)urther investigations will clarify whether EPS, a substance which is very active in vitro, will also be able to activate macrophages in vivo." Clearly, Stimpel provides no guidance whatsoever to *in vivo* applications, since the reference clearly states that those experiments have not yet been done.

Third, there is no indication by Stimpel that *E. purpurea* would be effective in an anti-coccidial application, since Stimpel tests the toxicity of EPS-stimulated macrophages against tumor cells, while coccidia are parasites. Again, the Examiner's attention is drawn to the last paragraph of the reference where Stimpel states that "(e)xperiments are in progress to test whether EPS-activated macrophages perform not only extracellular tumor cell killing, but also intracellular killing of parasites." Again, Stimpel provides no guidance with respect to effects against parasites such as coccidia, since those experiments have not yet been done.

Fourth, it is well recognized that in order for references to be combined for the rejection of claims under § 103, there must be some suggestion in the references for such a combination. It is strongly urged that there is no such suggestion in either of the references to combine them in order to reject the instant claims. There is nothing in Anderson that would suggest providing an herbal supplement to a poultry dietary regimen in order to enhance the response of the poultry immune system to an anticoccidial vaccine. With respect to Stimpel's teaching that a purified fraction of EPS extracted from *E. purpurea* has the

ability to stimulate macrophages *in vitro*, it is a considerable stretch for that teaching to be interpreted as providing the motivation to include *Echinacea* as a dietary supplement in poultry feed in order to enhance the immune response to an anticoccidial vaccine. Nothing in either reference could be interpreted by one of skill in the art to be of relevance to the other. Anderson doesn't suggest an adjuvant to enhance the reponse to the vaccine, and Stempel doesn't even mention immune response, avian vaccines or coccidia. Clearly, neither reference, either alone or in combination, teaches the elements of the rejected claims.

For these reasons, it is respectfully requested that the rejection be reconsidered and withdrawn.

In view of the above amendments and remarks, it is believed that the application is now in condition for allowance. Accordingly, it is respectfully requested that the rejections be withdrawn and that the application be allowed to issue. If there are any remaining issues to be resolved, the Examiner is invited to telephone the undersigned at the number below.

RECEIVED
JUL 15 2002
TECH CENTER 1600/2900

Respectfully submitted,

June 26, 2002
Date

Janelle S. Graeter, Patent Advisor
Registration No. 35,024
USDA-ARS-OTT
5601 Sunnyside Ave., Rm. 4-1159
Beltsville, Maryland 20705-5131
Telephone: (301) 504-5676

cc:
P. Allen
H. Silverstein

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, DC 20231, on June 26, 2002 (Date)

Allen et al.
(Name of applicant, assignee, or Registered Representative)

(Signature) 6-26-02 (Date)

Version with Markings to Show Changes Made

1. (Amended) A method for protecting poultry against coccidiosis, said method comprising inoculating chicks with an effective [immunization dosage] <u>amount</u> of an anticoccidial vaccine and providing a dietary regimen composition comprising an *Echinacea* supplement in an amount effective for enhancing an immune response to said vaccine and an ingestible carrier.